GROWTH HORMONE-RELEASING FACTOR AND ITS RECEPTORS IN AGING: RELEVANCE TO ALTERED HYPOTHALAMO-PITUITARY AXIS FUNCTIONS, P. Gaudreau, Neuroendocrinology Laboratory, Louis-Charles Simard Research Center, Notre-Dame Hospital and Department of Medicine, University of Montreal, Montreal, Canada

Growth hormone (GH) is released from the anterior pituitary into the circulation and contributes, either directly or through the action of insulin-like growth factor (IGF-I), to the maintenance of several tissue functions in adulthood. The pulsatile secretion of GH is regulated by two hypothalamic peptides, growth hormone-releasing factor (GRF) and somatostatin (SRIF). These peptides exert opposing actions on somatotroph cells by triggering specific G_s- and G_i-protein-coupled receptors. In middle age and old mammals, changes occur along the hypothalamo-pituitary GH axis, leading to a diminution of GH and IGF-I circulating levels. We have reported that a decrease in the number of high affinity pituitary GRF receptor binding sites appears early on in adult rats. This change precedes the diminution of GRF-induced GH secretion observed *in vivo* and *in vitro* in older animals. An increase in the number of low affinity GRF binding sites is seen thereafter, leading in old rats to a blunting of the high affinity binding sites and to an apparent reduction of the total number of sites. In addition, binding studies suggest that the GRF receptor develops a reduced ability to couple with its ligands and G-protein system. To further assess the importance of this receptor, we studied GRF binding in a rat model of successful aging. Interestingly, in rats submitted to a moderate calorie restriction from 8 to 18 months of age, pituitary GRF binding site parameters are similar in the old restricted and young control rats, while those of old *ad libidum* fed rats are deteriorated. Altogether, these results indicate that the pituitary GRF receptor status may play a significant role in the maintenance of the somatotroph function in aging. Molecular and immunological approaches will now be needed to elucidate some of the mechanisms involved in the modulation of GRF receptor sensitivity and functionality, in normal and successful aging.